Value and Implantation Risk of Thin Needle Aspiration Biopsy in The Diagnostic Malign Pulmonary Lesions

Akciğerin Malign Lezyonlarında İnce İğne Aspirasyon Biyopsisinin Tanısal Değeri ve İmplantasyon Riski

Needle Biopsy in the Lung Cancer
Akciğer Kanserinde İğne Biyopsisi

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Özet

Amaç

Çalışmamızın amacı, malign lezyonlarda ince iğne aspirasyon biyopsisinin tanısal değerini araştırmak, Chiba ile enjektör iğnesinin tanı sonuçlarını karşılaştırmak ve iğnenin geçtiği yerde malign hücre ekim olasılığını araştırmaktır.

Gereç ve Yöntemler

Kliniğimizde malignite ön tanısıyla opere edilen, yaş ortalaması 58.17 (38-75) olan 67'si erkek, 3'ü kadın toplam 70 olgunun cerrahi rezeksiyon materyaline ince iğne aspirasyon biyopsisi yapıldı. İnce iğne aspirasyon biyopsisi için 20-21 gauge kalınlıkta Chiba aspirasyon iğnesi ve 21gauge kalınlıkta enjektör iğnesi kullanıldı. Her bir cerrahi rezeksiyon materyalinin, Chiba ve enjektör iğneleri iç aspirat ve yine bu iğnelerin dış yüz sürüntü yaymalarının sitolojik sonuçları bu materyallerin histopatoloji sonuçları ile karşılaştırıldı.

Bulgular

Chiba iğnesi ile yapılan ince iğne aspirasyon biyopsisinde 70 materyalin 58'ine malignite, 1'ine benign tanısı konulurken, 11'ine tanı konulamadı. Enjektör iğnesiyle sonuçlarda 58'ine malign tanısı konulurken, 12'sine tanı konulamadı. Her iki teknikle yalancı pozitif sonuç alınmadı. İşlemin tanısal sensitivitesi Chiba ve enjektör iğnesi için sırasıyla %84 ve %82.8'dir. (p=0.077). Her iki iğne dış yüzeylerinin ayrı ayrı lama sürülmesi ile hazırlanan yaymalar incelendiğinde; chiba iğnesiyle hazırlanan 70 yaymanın 45'inde (%64.3), enjektör iğnesiyle hazırlanan 70 yaymanın 42'sinde (%60) malign hücre tespit edildi (p=0.6008).

Sonuç

Akciğerin malign lezyonlarında, seçilmiş olgularda ince iğne aspirasyon biyopsisi kolay uygulanabilir, tanı değeri yüksek bir yöntemdir.Tanısal verimlilik açısından her iki iğne arasında anlamlı bir fark yoktur. Tümör dokusuna yönelik herhangi bir girişim, özellikle ileri derecede sellüler ve malign tümörlere uygulandığında, iğnenin geçtiği yerde malign hücre implantasyonu için risk oluşturur.

Anahtar Kelimeler

Akciğer, İğne Biyopsisi, Malignite.

Abstract

Aim

The aim of our study was to investigate the diagnostic value of fine needle aspiration biopsy in malignant lesions, compare the results obtained by a Chiba and an injection needle and determine whether or not malignant cells are implanted on the course of the needle.

Material and Methods

Fine needle aspiration biopsy was done on the resected material from a total of 70 patients (67 male and 3 female) with a mean age of 58.17 years (range: 38-75 years) who underwent surgery for prediagnosed malignancy.For each surgically resected material, the cytological and histopathological findings of the internal aspirates from both the Chiba and injector needles as well as the smears from the external surfaces of these needles were compared.

Results

Of the 70 biopsy materials obtained by the Chiba needle, malignancy was demonstrated in 58, benign lesions in one, while 11 were non-diagnostic. The results obtained with the injector needle revealed 58 malignancies, and 12, without any diagnosis. With both techniques, no false positive results were observed. The diagnostic sensitivity of the techniques was 84% and 82% for the Chiba and injector needles respectively. Examination of the smears obtained from the external surfaces revealed malignant cells in 45 (64.3%) of the 70 smears obtained with a Chiba needle and 42 (60%) of the 70 smears obtained with an injector needle.

Conclusions

Fine needle aspiration is a method with high diagnostic value. It can be easily performed in selected cases with malignant pulmonary lesions. There were no significant differences between the two methods in terms of diagnostic yield. Any intervention targeting the tumor tissue, especially in advanced stage cellular and malignant tumors, carries a significant risk for implantation of malignant tumor cells on the course of the needle.

Keywords

Lung, Needle Biopsy, Malignancy.

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Introduction

Transthoracic needle biopsy (TTNB) is an effective diagnostic method with wide range of indications and limited contraindications for thoracic lesions [1, 2]. TTNB was first used in 1883 for isolation of the microorganisms from 3 patients with Leyden pneumonia, and by using this method, Menetrier was the first to diagnose pulmonary cancer [3]. Starting from the second half of the 20th century, the technique has become more popular for the last two or three decades with the introduction of radiological techniques that facilitate imaging in biopsy studies, increased experience of physicians and cytopathologists applying biopsy procedures, improved needle types, and increased ability to control complications [1].

Material and Method

The study involved surgical resection materials of 70 patients (67 male, 3 female; mean age: 58.17 years, age range: 38-75 years) planned for fine needle aspiration biopsy (FNAB). Patients were properly informed about the surgical procedure and a signed approval was received from every patient. The patients were operated in our clinic for prediagnosis of malignancies. For the fine needle aspirations, 20-21 gauge (G) Chiba aspiration needles and 21 gauge injectors were used. Fine needle aspirations were performed on the resected materials in pathology lab without any additional surgical procedure.

Immediately after the intraoperative resection procedure was completed, resected materials were evaluated without any formaldehyde fixation. Before the procedure, the materials were palpated with hand and the locations of the lesions were determined. The best point for FNAB was determined for each. The lesion was penetrated with Chiba aspiration needle through the location determined. When the desired depth was reached, introducer was withdrawn, and a 20 ml injector was attached to the outer tip of the needle. The needle was moved back and forth within the lesion for a few times while the piston was being retracted, creating a negative pressure and thus, continuous aspiration was achieved. The same procedure was repeated using another 20 ml injector and its own needle.

After the aspiration procedure was completed, the external surface of each needle was smeared on a separate glass plate for each needle without any contact of the needle to the plate. The aspiration material in the needle and injector was sprayed on separate plates. As soon as the smears were prepared, the slides were sent to the pathology laboratory. The smears prepared using the internal aspirations obtained with Chiba and injector needles were divided into two groups, and depending on the preference of the pathologist, the first half of the preparations were fixed in 70% alcohol and stained with hemotoxylene-eosin. The other half and slides prepared by smearing the external surface of the Chiba and injector needles were air-dried and stained with Giemsa.

The cytological evaluation of the preparations was made by an experienced pathologist, who was blinded to the histopathological diagnosis for resected materials. The histopathological evaluation of surgical resection materials was made by three different pathologists.

The cytological results of the inner aspirate obtained with Chiba and injector needles and the external smear cultures of each resection material were compared with the histopathological results of the same material. In the evaluation of the results, a malign diagnosis that could be established was regarded as 'true positive'; a diagnosis that was considered malign but turned out to be benign was regarded as 'false positive'; a benign diagnosis that could be established was regarded as 'true negative'; the undiagnosed ones were regarded as 'false negative'.

Results

In 38 (54.28%) patients, right thoracotomy and in 32 (45.72%) cases, left thoracotomy were performed. The distribution of the procedures applied were as follows: pneumonectomy in 27 patients (9 right, 18 left), upper lobectomy in 22 patients (16 right, 6 left), lower lobectomy in 12 patients (4 right, 8 left), bilobectomy superior in 2 patients; bilobectomy inferior in 5 patients, and wedge resection in 2 patients (right).

The distribution of the diagnoses established with FNAB (Chiba needle) for 70 surgically resected materials was as follows: malignant, 58 (82.85%) samples; benign, 2 (2.86%) samples; and no diagnosis, 10 (14.29%) samples. In 52 (89.6%) of 58 malignancies, small-celled lung cancer and lung cancer other than small-celled could be distinguished, while 6 lesions (10.4%) were considered malign only (Table 1).

The distribution of the diagnoses established with FNAB (injector needle) for 70 surgically resected materials was as follows: malignant, 58 (82.85%) samples; no diagnosis, 12 (17.15%) samples. In 49 (84.5%) of 58 malignancies, small-celled lung cancer and lung cancer other than small-celled could be distinguished, while 9 lesions (15.5 %) were considered malign only (Table 2).

Tablo 1. The cytological diagnoses of 70 surgical materials that were applied FNAB with a Chiba needle.

Diagnosis	Count	%
Squamous-celled carcinoma	24	34.28
Adenocarcinoma	12	17.14
Lung cancer other than small-celled	14	20.00
Small-celled lung cancer	2	2.86
Malignancy	6	8.57
Benign	2	2.86
Non-diagnostic	10	14.29

Histopathological evaluations of the postoperative surgical resection materials obtained from 70 patients revealed that the diagnosis of 69 samples was malign and of 1 sample, benign. Squamous celled carcinoma was

Tablo 2. The cytological diagnoses of 70 surgical materials that were applied FNAB with an injector needle.

Diagnosis	Count	%
Squamous-celled carcinoma	22	31.43
Adenocarcinoma	9	12.86
Lung cancer other than small-celled	16	22.85
Small-celled lung cancer	2	2.86
Malignancy	9	12.86
Benign	-	-
Non-diagnostic	12	17.14

the most common diagnosis (66%) for malign samples. This was followed by adenocarcinoma (23%).

The comparisons of histopathological results and cytological results of Chiba aspiration biopsy showed that the results were compatible for differentiation of small-celled lung cancer and lung cancer other than small-celled, while subgroups of lung cancer other than small-celled were not compatible in 5 lesions. Two squamous-celled carcinomas diagnosed by cytological evaluation were diagnosed as adenocarcinoma in the histopathological evaluation, while 3 adenocarcinomas diagnosed by cytological evaluation were diagnosed as 2 squamous celled carcinomas and 1 pleomorphic carcinoma. The samples that were found to be malign in FNAB cytology were compatible and thus, were considered 'true positive'. The sample histopathologically diagnosed as organized pneumonia was determined to be benign in cytological evaluations. Thus, it was considered 'true negative'. The samples that could not be diagnosed by cytological evaluations were considered 'false negative'. There were no 'false positive' results.

The comparisons of histopathological results and cytological results of injector needle aspiration biopsy similarly showed that the results were compatible for differentiation of small-celled lung cancer and lung cancer other than small-celled, while subgroups of lung cancer other than small-celled were not compatible in 2 lesions. Two squamous-celled carcinomas diagnosed by cytological evaluation were diagnosed as adenocarcinoma in the histopathological evaluation. The samples that were found to be malign in FNAB cytology were compatible and were considered 'true positive'. The samples that could not be diagnosed by cytological evaluations were considered 'false negative'. There were no 'false positive' results (Table 3).

Evaluation of the external smear cultures of both needles

Tablo 3. The cytological diagnoses of 70 surgical materials that were applied FNAB with an injector needle.

	Accuracy	Sensitivity (%)
Chiba needle	59/70	84.2
Injector needle	58/70	82.8

on different plates showed malign cells in 45 (64.5%) of 70 smears from China needles and 42 (60%) of 70 smears from injector needles (Table 4).

The histopathological results of the lesions with malign cells according to the cytological evaluation of external smear cultures from both needles were studied. Accordingly, the most common histopathological diagnosis for lesions with malign cells determined in the external smears from Chiba needles was squamous-celled carcinoma (65%), followed by adenocarcinoma (29%). Similarly, the most common histopathological diagnosis for lesions with malign cells determined in the external smears from injector needles was squamous-celled carcinoma (62%), followed by adenocarcinoma (33%).

Tablo 4. The results of cytological evaluation of the external smears of the Chiba and injector needles.

Diagnosis	Chiba Needle		Injector Needle	
	Count	%	Count	%
With malign cells	45	64.3	42	60
Without malign cells	25	35.7	28	40

Discussion

FNAB has high sensitivity and specificity rates. In previous studies, the sensitivity for malign diseases was reported to be 64-97 %. For benign lesions, however, this rate was reported to be 11.7-68% [3]. In the studies by Stanley, Khouri, and Green, the sensitivity rates of FNAB for malignancy were determined as 96.6%, 96%, and 97% [4-6]. On the other hand, for benign lesions, the sensitivity of the method was found to be 68% by Khouri, 44% by Green, and 11.7% by Johnson [5-7]. In our study, the sensitivity rate of FNAB for malign lesions was 84% with Chiba needle and 82.8% with injector needle (p=0.077), which is compatible with the literature. No statistically significant differences were determined between the two needles for diagnostic efficiency.

In primary lung carcinoma, tumor cell type is important for determination of prognosis and proper treatment. Numerous studies have shown compatible diagnoses with cytological and histopathological studies [3, 7, 8]. In most of these studies, only some of the cytological diagnoses could be compared with histopathological diagnoses. In our study, however, all the cytological diagnoses were compared with the postoperative histopathological diagnoses, and the results were confirmed. In our study, in the cytological evaluation of 70 surgically resected materials that were performed FNAB with Chiba needles, 58 lesions (82.85%) were diagnosed as malignant. Of these, the types of 38 lesions (65%) were definitely determined, and 52 lesions (89.6%) were differentiated as small-celled lung cancer or lung cancer other than small-celled. Six lesions (10.4%) were considered malign only.

The compatibility rate of cytopathological and histopathological diagnoses was 100% for small-celled lung cancer or lung cancer other than small-

celled, 91% for squamous-celled carcinoma, and 75% for adenocarcinoma. The cytological evaluation of 70 surgically resected materials that were performed FNAB with injector needles revealed that 58 lesions (82.85%) were malignant. Of these, the types of 33 lesions (56%) were definitely determined, and 49 lesions (84.4 %) were differentiated as small-celled lung cancer or lung cancer other than small-celled. Nine lesions (15.6 %) were considered malign only. The compatibility rate of cytopathological and histopathological diagnoses was 100% for small-celled lung cancer or lung cancer other than small-celled, and adenocarcinoma, and 90% for squamous-celled carcinoma.

The location and size of a lesion are believed to affect the diagnostic value of FNAB. Layfield et al have reported that the larger the lesion is, the higher the diagnostic value of FNAB [9]. Westcott, on the other hand, reported false negative results for all the lesions smaller than 2 cm [8]. Severe tumor necrosis and areas with severe inflammation, fibrosis, or pneumonia around the tumor may cause negative results [1, 4].

Radiological tools such as fluoroscopy, US, and CT increases the diagnostic value of the FNAB method. Dash et al have found a sensitivity rate of 97% for FNAB guided by CT and 90% for FNAB that was not radiologically guided [10]. In our study, FNAB was performed directly on palpable, surgically resected material, and thus, factors such as the location and size of the lesion and radiological guidance did not affect the diagnostic value of FNAB.

Due to complications of thick and sharp needles such as bleeding, which may rarely be fatal, today fine needles (19 G or thinner) are preferred. On the other hand, it has been reported that with sharp needles of large diameter, it is more likely to obtain sufficient material [1, 3], while with needles of smaller diameter, diagnostic efficiency was not found to be as low as expected [1, 11].

False negative results are an important problem for fine needle aspiration biopsy. Whereas in malign lesions, repetitions of the procedure in the same session increases the diagnostic yield by 35-45%, a negative result does not completely rule out malignancy [1,3]. The primary reasons for false negative results is insufficient sampling, inability to penetrate the lesion, severe necrosis in the lesion, biopsy from areas of inflammation or pneumonia, excessive aspiration of hemorrhage and technical issues. In FNAB with Chiba and injector needles, the rates of false positivity were 15.7% and 17%. Comparisons of the postoperative histopathological results of these lesions showed that 11 lesions (91.6%) were squamous-celled carcinoma and 1 lesion (8.4%) was benign. Almost all of the false negative results were detected for squamous-celled carcinomas. This shows how much the cavity forming characteristic of squamous-celled carcinoma and FNAB performed with the guidance of CT, which is effective in differentiation of the cavity area, affects the diagnostic yield.

The rate of false positive results with FNAB (0.025% - 2.4%) is very low. Various factors that may lead to false positive results are granulomatous reaction, organized pneumonia, pulmonary infarct, radiation and chemotherapy applications. In our study, no false positive results were determined with either of the needles.

The most common complications of FNAB are pneumothorax (5-61%), hemorrhage and hemoptisis (3-10%) [1, 3, 12,13]. The implantation and diffusion of the tumor cells on the course of the needle are the rare but serious complications, which are highly debated. Despite difficulty in determining the mechanism of implantation, it has been thought to be associated with such factors as use of needles with large diameters and sharp tips as well as synergic effects of tumors with high degree of malignancy. However, malign diffusion with FNAB has been reported recently [14]. Studies have shown that the number of tumor cells that implant on the course of the needle is relative to tumor redifferentiation. In obtaining diagnostic material from malign tumors with FNAB, tumor cell diffusion is inevitable. Indeed, malign cells were determined in smears of the external surfaces of the needles that were used in biopsy procedure on the resected materials. After fine needle biopsy procedures performed on 70 surgical materials, in 45 (64.3%) of the smears of the external surfaces of the Chiba needles and in 42 (60%) of the smears of the external surfaces of the injector needles, there were malign cell (p=0.6008).

Then, do all the malign cells on the external surface of the needle cause implantation on the course of the needle? Earlier studies showed that despite dispersion of millions of cells from a single tumor, very few can lead to metastasis or invasion because in a heterogeneous tumor, subclones with a potential for metastasis must be formed first. The cells in this particular clone gain molecular characteristics that will allow vascular diffusion and implantation of these cells into that medium by extracellular matrix invasion. Even when there are cells with this caharcteristics on the transthoracic biopsy needle, the medium must allow for multiplication of these cells [15]. Thus, despite evidence of more than 90% malign cells on the course of the needle in the experimental studies, the clinical incidence of malignancy is under 1 % [16]. It is known that in transthoracic needle biopsy procedures, particularly for severely cellular and malign tumors, the risk of implantation is increased. The most common view is when possible, the removal of the course of the needle after the biopsy procedure. This has been in general suggested at the time of tumor removal [17].

Conclusion

The diagnostic sensitivity of the technique was 84% and 82% for the Chiba and injector needles respectively and there are no differences between the two needles for diagnostic yield. In fine needle aspiration biopsy procedures applied on peripheral lesions that can be

accessed by a needle, injector needles may be preferred because they are inexpensive and easily accessible. Malign cell implantation on the course of the needle is a rare but serious complication of transthoracic needle biopsy. After FNAB procedures, malign cells were determined in 64.35 of the external surface smears of the Chiba needles and in 60% of the external surface smears of the injector needles. Any FNAB intervention to tumor tissue, particularly to high cellular and malign tumors, poses a risk of malign cell implantation on the course of the needle. Thus, in operable patients with high potential for malignancy whose lesions can be resected, transthoracic needle biopsy should be avoided. If such patients are performed a needle biopsy and then operated, the course of the needle should also be removed along with the tumor.

References

1. Salazar AM, Westcott JL: The role of transthoracic needle biopsy for the diagnosis and staging of lung cancer. In: Matthay RA (ed): Clinics in Chest Medicine, 1993; 14:99-110.
2. Cham MD, Lane ME, Henschke CI, Yankelevitz DF: Lung biopsy: special techniques. Semin Respir Crit Care Med. 2008; 29:335-349.
3. Weisbrod GL: Transthoracic needle biopsy. World J Surg. 1993; 17:705-711.
4. Stanley JH, Fish GD, Andriole JG, Gobien RP, Betsill WL, Laden SA, Schabel SI: Lung lesions: Cytologic diagnosis by fine needle biopsy. Radiology 1987; 162:389-391.
5. Khouri NF, Stitik FP, Erozan YS,Gupta PK, Kim WS, Scott WW JR, Hamper UM, Mann RB, Eggleston JC, baker RR: Transthoracic needle aspiration biopsy of benign and malignant lung lesions. AJR 985; 144:281-288.
6. Greene R, Szyfelbein WM, Isler RJ, Stark P, Janstsch H : Supplementary tissue-core histology from fine needle transthoracic aspiration biopsy. AJR 1985; 144:787-792.
7. Johnston WW: Percutaneous fine needle aspiration biopsy of the lung: A study of 1,015 patients. Acta Cytol 1984; 28:218-224.
8. Westcott JL: Direct percutaneous needle aspiration of localized pulmonary lesions: results in 422 patients. Radiology 1980; 137:31-35.
9. Layfield LJ, Coogan A, Johnston WW, Patz EF: Transthoracic fine needle aspiration biopsy: Sensitivity in relation to guidance technique and lesion size and location. . Acta Cytol 1996; 40:687-690.
10. Dash BK, Tripathy SK: Comparison of accuracy and safety of computed tomography guided and unguided transthoracic fine needle aspiration biopsy in diagnosis of lung lesions. JAPI 2001; 49:626-629.
11. Zavala DC, Schoell JE: Ultrathin needle aspiration of the lung in infectious and malignant disease. Am Rev Respir Dis 1981; 123:125-131.
12. Zavala DC, Bedell GN: Percutaneous lung biopsy with a cutting needle. Am Rev Respir Dis 1972; 106:186-193.
13. Khan MF, Straub R, Moghaddam SR, Maataoui A, Gurung J, Wagner TO, Ackermann H, Thalhammer A, Vogl TJ, Jacobi V: Variables affecting the risk of pneumothorax and intrapulmonary hemorrhage in CT-guided transthoracic biopsy. Eur Radiol. 2008;18:1356-1363.
14. Sacchini V, Galimberti V, Marchini S, Luini A: Percutaneous transthoracic needle aspiration biopsy: a case report of implantation metastasis. Eur J Surg Oncol 1989; 1:179-183.
15. Cotran RS, Kumar V, Collins T: Robbins Pathologic Basis of Disease. Sixth edition, W.B. Saunders Co, Philadelphia 1999; pp260-329.
16. Seyfer AE, Walsh DS, Graeber GM, Nuno IN, Eliasson AH : Chest wall implantation of lung cancer after thin needle aspiration biopsy. Ann Thorac Surg 1989; 48:284-286.
17. Ryd W, Hagmar B, Eriksson O: Local tumour cell seeding by fine-needle aspiration biopsy. A semiquantitative study. Acta Path Microbiol Immunol Scand Sect A 1983; 91:17-21.